

**REMARKS**

**Status of the Claims**

Claims 1, 2, 6, 9-11, 13, 17, 35, 38, 40, 49, 50, 115 and 131-134 are currently pending in the application. Claims 1-4, 6, 7, 9, 130 and 131 stand rejected. Claims 10, 11, 13, 17, 35, 38, 40, 49, 50, 115 and 132-134 are withdrawn as being drawn to a non-elected invention. Claims 1 6, 9 and 131 have been amended. Claims 3, 4, 7 and 130 have been cancelled. All amendments and cancellations are made without prejudice or disclaimer. No new matter has been added by way of the present amendments. Specifically, the amendment to claim 1 is supported by at least claim 7, now cancelled, and the specification at, for instance, page 30, and page 46. Amendments to claims 6 and 9 are to make these claims consistent with the amendments made to claim 1. Reconsideration is respectfully requested.

**Rejections Under 35 U.S.C. § 112, First Paragraph**

**Written Description**

Claims 1-4, 6, 9, 130 and 131 stand rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement. (*See*, Office Action of November 23, 2007, at pages 3-4, hereinafter, “Office Action”). Claims 3, 4 and 130 have been cancelled herein, thereby obviating the rejection of these claims. Applicants traverse the rejection as to the remaining claims.

The Examiner states that the specification discloses only a C-to-T mutation at position - 7351/2228 of the t-PA locus. (*Id.* at page 3). The Examiner concludes that the claimed genus of mutations is not sufficiently supported by the specification. (*Id.* at pages 3-4).

Although Applicants do not agree that the presently claimed invention lacks written description support in the specification, to expedite prosecution, claim 1 has been amended to recite the limitations of claims 3, 4 and 7, which previously encompassed mutation at the t-PA locus at position -7351, wherein said mutation is a cytosine to thymine mutation.

Since claim 7 was not rejected as lacking written description support, and since the specification clearly discloses at least this mutation as being linked to the claimed diseases, and since the Examiner has admitted in the Office Action that at least this subject matter is supported, Applicants believe that at least amended claim 1 is fully supported in the specification in such a manner as to convince one of skill in the art that they were in possession of the claimed invention.

Since no specific reasoning is set forth by the Examiner for the rejection of dependent claims 2, 6, 9 and 131, these dependent claims are believed to also be supported by the specification as, *inter alia*, depending from a fully supported base claim, amended claim 1.

Reconsideration and withdrawal of the written description rejection of claims 1, 2, 6, 9 and 131 are respectfully requested.

#### Enablement

Claims 1-4, 6, 9, 130 and 131 stand rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the enablement requirement. (*See*, Office Action, at pages 4-8). Claims 1 and 131 are additionally rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement based on separate and distinct grounds from the first enablement rejection. (*Id.* at pages 8-13).

Claims 3, 4 and 130 have been cancelled herein, thus obviating the rejection of these claims.

Applicants traverse the rejection as to the remaining claims.

The Examiner states that the specification fully enables “a method of identifying a subject predisposed to ischemic stroke, comprising identifying the C-to-T mutation at position -7351/2228 of the t-PA locus in the subject.” (*Id.* at page 4). However, the Examiner further states that the specification does not enable a similar method comprising identifying any mutation in the subject that reduces the release of t-PA. (*Id.*).

Additionally, with respect to claims 1 and 131, the Examiner states that these claims are enabled for “a method of identifying a subject at increased risk for ischemic stroke (by identifying that his rate of release of t-PA is reduced).” (*Id.* at page 8). However, the Examiner further states that the specification does not enable a similar method in which such a patient is treated for ischemic stroke or for preventing such an incident. (*Id.*).

Although Applicants do not agree that the claims lack enablement, to expedite prosecution, as noted above, claim 1 has been amended to recite the mutation in the t-PA locus which the Examiner agrees is supported by the present specification. Since claim 1 now is believed to encompass the subject matter the Examiner has identified as being enabled, Applicants believe this rejection is traversed at least with respect to claim 1.

Additionally, claim 131 is amended to recite, in part, “The method according to claim 1, wherein determining the presence of the mutation in the subject thereby (i) indicates that the subject is suitable for ischemic stroke interventive therapy ...” Thus, claim 131 is not directed to “identifying a subject in whom ischemic stroke can be prevented or treated” as indicated by the

Examiner. Rather, claim 131, as amended, recites that determination of the presence of the mutation indicates that the subject is suitable for ischemic stroke interventive therapy.

Since no independent reasoning is provided by the Examiner for the rejection of dependent claims 2, 6 and 9, these dependent claims are also believed to be enabled for, *inter alia*, depending from an enabled base claim, amended claim 1.

Reconsideration and withdrawal of the enablement rejection of claims 1, 2, 6, 9 and 131 are respectfully requested.

### **Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 1-4, 6, 7, 9, 130 and 131 stand rejected under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. (*See*, Office Action, at pages 13-14). Claims 3, 4, 7 and 130 have been cancelled herein, thereby obviating the rejection of these claims. Applicants traverse the rejection as to the remaining claims.

The Examiner states that “Applicants’ invention appears to be the discovery of a point mutation associated with a decreased level or expression of t-PA, as measured in cell culture experiments,” but that the claims instead recite “determining the rate of release of t-PA in a subject and identifying a subject having a reduced rate of release of t-PA.” (*Id.* at page 13). The Examiner requests clarification.

Although Applicants do not agree that the claims are indefinite, to expedite prosecution, claim 1 has been amended to recite, in part, “determining the presence of a mutation in the subject that reduces the release rate of tissue plasminogen activator, wherein said mutation is a

cytosine to thymine mutation at position -7351 of the upstream region of the tissue plasminogen locus.” Thus, the amendment clarifies that the point mutation is associated with a reduced release rate of t-PA.

Since no specific reasoning is provided for the rejection of dependent claims 2, 6, 9 and 131, these claims are believed to also be definite for, *inter alia*, depending from a definite base claim, amended claim 1.

Reconsideration and withdrawal of the indefiniteness rejection of claims 1, 2, 6, 9 and 131 are respectfully requested.

### **Rejections Under 35 U.S.C. § 102(b)**

Claims 1, 3, 6, 9, 130 and 131 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Kluft et al., WO 97/07240 (hereinafter referred to as “Kluft et al.”). (See, Office Action, at pages 14-15). Claims 3 and 130 have been cancelled herein, thereby obviating the rejection of these claims. Applicants traverse the rejection as to the remaining claims.

Although Applicants do not agree that the claims are anticipated by Kluft et al., to expedite prosecution, as noted above, Applicants have amended claim 1 to recite the limitations of non-anticipated dependent claim 7. Claim 7 is now cancelled. Applicants believe claim 1, at least as amended, recites limitations not disclosed in Kluft et al. Thus, Kluft et al. cannot anticipate claim 1. Anticipation requires that “each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” (See, *In re Robertson*, 169 F.3d 743, 745, 49 U.S.P.Q.2d 1949 (Fed. Cir. 1990), quoting *Verdegaal Bros., Inc. v. Union Oil Co.*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987)).

Dependent claims 6, 9 and 131 are not anticipated as, *inter alia*, depending from a non-anticipated base claim, amended claim 1.

Reconsideration and withdrawal of the anticipation rejection of claims 1, 6, 9 and 131 are respectfully requested.

### **Rejections Under 35 U.S.C. § 103(a)**

Claims 1-4, 6, 9, 130 and 131 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kluft et al. in view of Bulens et al., *J. Biol. Chem.*, 270(13):7167-7175, 1995 (hereinafter, “Bulens et al.”). (*See*, Office Action, at pages 15-16). Claims 3, 4 and 130 have been cancelled herein, thereby obviating the rejection of these claims. Applicants traverse the rejection as to the remaining claims.

Again, as noted above, although Applicants do not agree that the presently claimed invention is obvious in light of the combined disclosure of the cited references, to expedite prosecution, claim 1 has been amended to recite the limitations of non-obvious dependent claim 7. Claim 7 is now cancelled. Applicants believe that claims 1, at least as amended, and 2, depending therefrom, are non-obvious because they recite (or incorporate by dependency) limitations that are neither disclosed nor suggested by the cited references.

Since no independent reasoning is provided by the Examiner for the rejection of dependent claims 6, 9, and 131, these claims are also believed to be non-obvious for, *inter alia*, depending from a non-obvious base claim, amended claim 1.

Reconsideration and withdrawal of the obviousness rejection of claims 1, 2, 6, 9 and 131 are respectfully requested.

Application No. 10/563,360  
Amendment dated May 22, 2008  
Reply to Office Action of November 23, 2007

Docket No.: 0641-0278PUS1

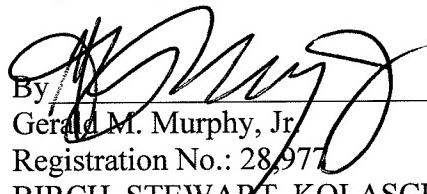
## CONCLUSION

If the Examiner has any questions or comments, please contact Thomas J. Siepmann, Ph.D., Registration No 57,374, at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

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Respectfully submitted,

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